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VISUALLY INDUCED OCULAR TORSION

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ABSTRACT

There has been some controversy whether ocular torsion (eye rotation around the line of sight) is induced in response to a tilted visual scene. The aim of this thesis was to investigate if ocular torsion can be induced by viewing a tilted visual scene and to evaluate the effect of different stimuli parameters on the torsional response. In three different studies, eye movements were recorded binocularly with a modern head mounted video system on healthy individuals. The stimuli (photos with spatial clues and abstract images) where displayed on a screen or a LCD in front of the test subjects.

All subjects responded with a torsional movement in the same direction as a static tilted stimulus. The response amplitude was small, only compensating for a minor portion of the stimuli tilt. The response was well conjugate for the right and left eye. In the first study, a visual scene enriched with spatial clues important for maintaining posture was found to induce significantly more torsion compared to a scene without spatial clues. The degree of stimuli tilt had no significant effect, nor the stimuli periphery. In the second study, torsional response was shown to decay and return towards the initial baseline, similar to an adaptation, when a tilted stimulus was viewed for several minutes. In the third study, subjects were presented with a stimulus that was alternatively tilted (position change) or turned (motion change) in conflicting directions. The response varied depending on which stimulus was presented first. When starting with stimulus motion the position stimulus was neglected. When starting with a position stimulus the stimulus motion was neglected.

In conclusion, a tilted visual scene does induce ocular torsion. The response is conjugate and it rotates the eyes in a compensatory direction. The torsional amplitude is small but becomes larger if the stimulus has spatial clues. The response is not maintained over time and it can be cancelled by a previous response.

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LIST OF PUBLICATIONS

I. Pansell T, Sverkersten U, Ygge J
Visual spatial clues enhance ocular torsion response during visual tilt
Experimental Brain Research, 2006 Nov; 175(3):567-74

II. Sverkersten U, Ygge J, Pansell T
Drift of Visually Induced Optostatic Torsion
Strabismus, 2009; 17(2):82-89

III. Sverkersten U, Öqvist Seimyr G, Ygge J, Pansell T
A rotatory step-ramp paradigm reveals different motion detecting mechanisms for visually induced ocular torsion
Submitted

CONTENTS

LIST OF ABBREVIATIONS

CCW	Counter Clock-Wise
CW	Clock-Wise
CNS	Central nervous system
C-SC	Circular-Spatial clues
Deg	Degree
EOM	Extra Ocular Muscle
ETD	Eye Tracking Device
fMRI	functional Magnetic Resonance Imaging
LCD	Liquid Crystal Display
LED	Light-Emitting Diode
Min	Minute
OCR	Ocular Counter Roll
OT	Ocular Torsion
PET	Positron Emission Tomography
RS	Ramp-Step
S-NSC	Square-No Spatial clues
SR	Step-Ramp
S-SC	Square-Spatial clues
Sec	Second
VOG	Video Oculography
VOR	Vestibulo Ocular Reflex

1 BACKGROUND

Our ability to stand up and maintain balance is crucial to everyday life. Visual, vestibular and proprioceptive information is integrated to perceive body posture and body movements in the central nervous system (CNS). The visual system is particularly important for distinguishing visual motion for sensing head movements in relation to visual objects nearby and to correctly perceive the visual surroundings for spatial orientation. The vestibular system in the inner ear is specialized in sensing the position and movements of the head in space. The proprioceptive system with mechanoreceptors in muscles, tendons and joints senses the position and movements of the body. Normal human subjects make variable intra-and inter individual use of the sensory input for maintaining balance (Guerraz et al. 2001; Lopez et al. 2006) and to correctly determine our position relative our surrounding (Witkin 1959; Asch et al. 1992).

1.1 VISION AND VISUAL MOTION

Visual motion is important for detecting moving objects as well as correctly distinguishing our own movement relative to the surrounding. Motion can be perceived directly, from the analysis of retinal motion that differs in luminance from the background (first order motion), from a moving contour that does't differ in luminance (second order) or indirectly, by extracting and locating features in the visual field and then analyze whether their location has changed over time (third order motion, feature tracking; Derrington et al. 2004). The underlying mechanisms of those motion detection mechanisms are different. Motion detection and feature recognition in primates are known to be processed in the dorsal and ventral streams, respectively (Livingstone et al. 1987; Zeki et al. 1988). While first order motion is characterized by a bottom-up input from the retina towards the visual cortex the feature tracking is more complex and influenced by both bottom-up and top-down components (downstream from higher cortical levels). The perceived motion can thus be modified depending on which feature values the subjects are attending to (Lu et al. 1995).

When a person moves, the perceived visual surrounding will move and shift position on the retina. For example, when turning the head to the right the visual surrounding will synchronously be shifted towards the left with the same amount as the head movement. When looking up, the visual field will be shifted downwards with the same amount as

the head movement. The perceived visual motion during head movements is termed *optic flow* and is a strong predictor for the postural system to interpret if the head is moving in relation to the visual surrounding. When driving a car with the eyes fixating a distant target straight ahead the visual optic flow will from the fixation target expand outwards with an optic flow velocity depending on the forward speed. The optic flow thus changes characteristics depending on if the person rotates or moves linearly in the surrounding.

1.2 VISUAL-VESTIBULAR INTERACTIONS

While stimulited to optic flow its possible to either perceive oneself as stationary observing a moving stimulus or perceive oneself as a moving in relation to a stationary stimulus. The illusion of self-motion is very strong and reveals the strong coupling between the visual and vestibular systems. Information from both the visual, vestibular and proprioceptive systems are sometimes necessary to correctly distinguishing between self- motion and the motion of surrounding (i.e. vection).

It has been shown that a stimulus moving in the peripheral visual field elicits a sensation of self-motion wheras if the stimulus is stimulating the central visual field elicites the sensation of beeing stationary in a moving surrounding (Brandt et al. 1973). A subject viewing a stimulus rotating in the frontal plane will after a while perceive whole-body rotation (roll vection) and a sensation of body tilt in the opposite direction to the rotatory stimulus. This is due to a conflict between the visual and vestibular sensory channels important for detecting body position and motion (Thilo et al. 1999). The sensation of self-tilt can also be elicited when looking at a tilted visual frame (Ebenholtz et al. 1977; Sigman et al. 1978). Positron Emission Tomography (PET) and fMRI studies have shown that a large-field motion stimulus not only activates the visual cortex but also deactivates the parietoinsular vestibular cortex. This finding led to the functional hypothesis that inhibitory reciprocal visual- vestibular interaction is a form of sensory integration for orientation in space and perception of motion (Brandt et al. 2002).

1.3 VISION AND THE NEED FOR EYE MOVEMENTS

The human retina has basically two different types of photoreceptors, rods and cones. In the fovea the cone density is high and the receptive fields are small allowing for high resolution vision. The cones are further divided into different types depending on the

maximum sensitivity to different wavelengths. This enables the visual system to distinguish colors in daylight. Visual acuity is highest in the central 1 degree of the retina, i.e. the fovea, and declines steeply more peripherally. In the peripheral retina cone density decreases and rod density increases. While the central retina is concerned with detailed color vision the peripheral retina is more concerned about detection. The rods are sensitive in dim conditions, to luminance contrast and to motion. For vision to work optimally the light has to be focused into a sharp image on the retina and the image has to be kept fairly stable onto the fovea. Light that is focused in front or behind the retina or an image, which is not kept stable onto the fovea will essentially lead to the percept of a blurry image.

Eye movements are required for primarily two reasons. Since only the fovea can distinguish small details this small part of the retina has to scan the visual scene to construct a mental image of a visual scene enriched with details. The other reason is due to the slow processing of the retina. The image on the retina has to be kept fairly stable; otherwise the visual percept will be interpreted as blurry. There will be more details about those two classes of eye movement below, but first a short description of the oculomotor plant and the innervation to the extraocular muscles.

1.3.1 The eye bulb and extra ocular muscles

The eye bulb is suspended in the orbital cavity by fascias, tendons, orbital fat, extra ocular muscles and the eyelids. The supporting tissues allow the eye bulb to rotate around its geometrical centre without moving within the orbital cavity (von Noorden 1996). The main component of the fascia is the Tenons capsule, which is continuous with the dural sheet surrounding the optic nerve. Tenons enter the orbit and fuses with the conjunctiva 1 mm from the ocular limbus. The six extra ocular muscles penetrates Tenons capsule and insert onto the eye bulb. The four rectus muscles and the superior oblique muscle originate from the apex of the orbital cone and the inferior oblique muscle from the floor (maxillary bone) of the orbit. The rectus muscles attach at the eyebulb at different distances from the limbus. The oblique muscles insert posterior to the equator of the globe (von Noorden 1996).

All eye muscles are approx. 40 mm long and consist of an orbital muscle fiber layer and a global muscle fiber layer; the two are separated by perimysium (Porter 1995). The characteristics of the muscle fibers of the orbital layer allows for a rapid response,

which is necessary for rapid eye movements. The global layer characteristics allow for a graded response, which is necessary for slow, precise eye movements and for tonic activation necessary for gaze fixation.

Smooth muscle fibers in Tenons capsule, the so called fibro muscular pulleys, have been shown to exert an effect on the position of the EOMs in the orbit and thus the effect on the eye rotations. The finding of the pulley system has attracted great interest from several research groups and several studies have been conducted to better understand the role of the pulley system on the eye movement control and how these pulleys are innervated (Demer 2000; Demer 2006).

1.3.2 Eye rotations and the orbital cavity

The medial walls of the two orbits are approximately parallel to each other while the lateral walls of the orbits are directed about 45-degrees laterally. The actions of the EOM depend on the position of the eye at the time of muscle contraction. This determines and explains the primary, secondary and tertiary actions that the EOM has on the globe. By this anatomy the action of the two recti muscles (superior and inferior) are solely elevation when the eyes are pointing in a 23 degree lateral direction but when looking straight ahead the action of these recti are also more complex. The superior rectus thus has an adducting action together with an intorsion action while the inferior rectus muscle has also an adduction action together with an extorting effect, the primary position of the eye is approximately 23-degrees nasal to the position of the orbit.

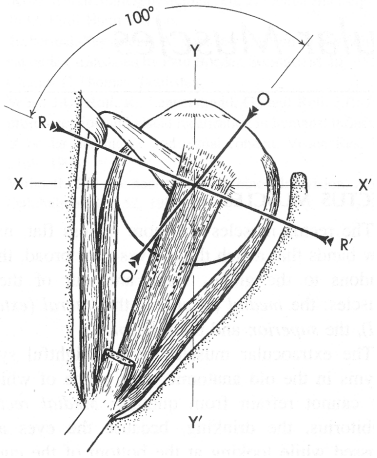

Figure 1. Illustration of the orbital cavity and the eye bulb with the extra ocular muscles as seen from above. It is worth to note the direction of the visual axis (Y-Y´) and the relationship to the pulling direction of the extra ocular muscles (O-O´;R-R`; Binocular vision and ocular motility, Von Noorden)

Eye movements are described as rotations around three orthogonal axes. A rotation around the horizontal axis makes vertical eye movements. A rotation around the vertical axis makes horizontal eye movements and, a rotation around the anterio-posterior axis makes torsional eye movements

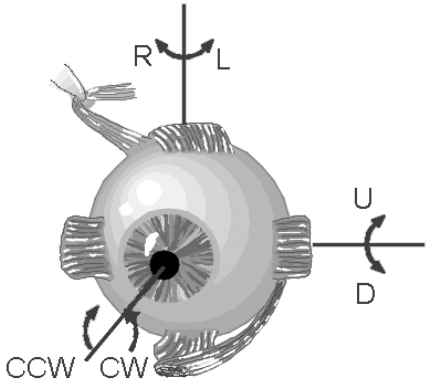

Figure 2. Frontal view of the eye with the rotation axes. Right- (R) and leftward (L) movements are rotated around the vertical sagittal axis. Upward (U) and downward (D) movements are rotating around the horizontal coronal axis (D) and counter clock-wise (CCW) and clock-wise (CW) movements are rotating around the anterior- posterior axis (from Tutis Vilis homepage).

Intorsion occurs when the superior part of the cornea rotates towards the nose. Extorsion occurs when the superior cornea rotates away from the nose. The superior oblique muscle is the primary muscle for intorsion in straight ahead gaze and in abduction. The inferior oblique muscle is the primary muscle for extorsion in straight ahead gaze and in abduction. When the eye is adducted the primary muscles for in- and extorsion are the superior rectus muscle and inferior rectus muscle respectively.

1.3.3 Neural innervation and control of eye movements

Three cranial nerves are innervating the six extra ocular muscles. The oculomotor nerve (n.III) is the largest and innervates four muscles, the inferior rectus (IR), medial rectus (MR), superior rectus (SR) and the inferior oblique (IO). The trochlear nerve (n.IV) innervates the superior oblique muscle (SO) and the abducent nerve (n.VI) innervates the lateral rectus muscle (LR).

To move the eye it is necessary to overcome the elastic restoring forces imposed by the orbital supporting tissues. The mechanical resting position of the eye is close to the primary position (straight ahead looking). To move the eye away from this primary position the initial nerve activity has to be large enough to overcome the elastic restoring forces as well as accelerating the eye bulb. This initial neural response is

termed the pulse of innervation. For the eye to maintain in an eccentric position the eye has to be kept there and to overcome the restoring forces. This requires less muscle force and thus less innervation compared to when accelerating the eye but still more innervation compared to when the eye is close to the primary position (Seidman et al. 1995). This level of innervation is called the step of innervation. A neural network integrates velocity coded signals into a position coded signals, this network is called the neural integrator (Robinson 1975). Ocular motor neurons carry information about both eye position (step) and velocity (pulse), thus a combined pulse-step signal (Robinson 1970). All conjugate eye movements and vergence eye movements have velocity and position components coded by neural integrators.

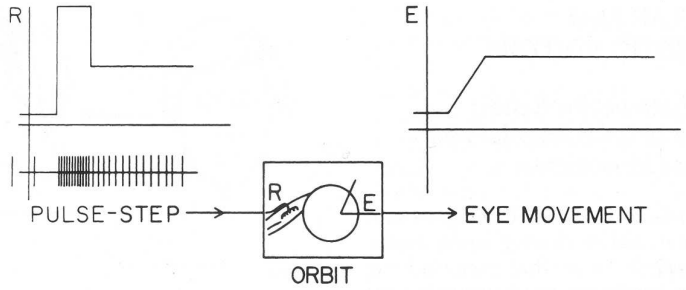

Figure 3. The neural signal for a saccade. At right is shown the eye movement: E is eye position in the orbita; the abscissa scale represents time. At left is shown the neural signal sent to the extraocular muscles to induce the saccade. The graph shows the neuron's discharge rate (R) against time (firing frequency histogram). Below, the occurrence of action potentials of an ocular motor neuron indicated as vertical lines. It shows the neurally encoded pulse (velocity command) and step (position command). Used by permission from Oxford University Press, Inc. (From The neurology of eye movements, Leigh and Zee)

If the integrator does not function perfectly, the eye position signal decays with time and the integrator is said to be "leaky" (Robinson 1975). The integration of torsional eye movements is less clear than for saccades. It is for example controversial if otolith signals during head tilt needs integration or if the otolith signal is linearly related to the degree of head tilt with no adaptation. It has however been shown that the counter-rolled eye position slowly drifts back towards the reference position during a sustained head tilt (Pansell et al. 2005). The underlying mechanism of this drift is not clear.

1.3.4 Functional classes of eye movements

There are several types of eye movements with different purposes and varying neural complexities. The two main classes of eye movements are those shifting the gaze and those stabilizing the image on the retina. Saccades belong to the group of gaze shifting eye movements. Saccades are high velocity eye movements moving the fovea over the visual field in a scanning pattern. Saccades are important for enlarging the field for

detailed vision since we only can see small details with a small central part of the visual field. Vision is suppressed during a saccade and thus not involved in visual processing like the category of stabilizing eye movements. In this thesis we will focus on the latter category with stabilizing eye movements.

1.4 STABILIZING EYE MOVEMENTS

Since we are moving almost all the time there is a constant requirement for the image to be stabilized on the retina. If the image is not kept still enough vision would be degraded and perceived as blurry. Defect stabilizing eye movements would preclude clear vision during walking, running, riding a bike, inducing a jumping visual field (i.e. oscillopsia) for each heel strike etc. To be able to compensate for head movements and to induce correct stabilizing eye movements the brain needs to integrate sensory information from the vestibular, visual and proprioceptive sensory organs to sense the head displacement with a high accuracy. Then, with an extremely short latency, induce a close to perfect amount of innervation to the EOMs to rotate the eye to move the retina with the same amount of displacement as the image motion (i.e. slow phase). The stabilizing eye movements consists of a repetitive to-and-fro movement with a visual motion matching component (slow phase) in the same direction as the visual motion and then a fast re-setting component (quick phase) in opposite direction to the visual motion. This repetitive eye movement is close to perfect for short lasting head rotations where the slow phase of the r-VOR (see below) has a gain (eye velocity/head velocity) of approx. 1.0 for head rotations up to 400 deg/sec. For pure visual motion (without head movements) the gain of the OKN (see below) is lower, approx. 0.8 for velocities less than 60 deg/sec (Pulaski et al. 1981).

1.4.1 Vestibular system and the vestibulo-ocular reflex (VOR)

The vestibular organ in the inner ear is specialized in sensing the head displacement as components of head rotations and head translations. The underlying mechanism for this visual stabilization mechanism most likely has its origin in the vestibular system (Raphan et al. 1979; Waespe et al. 1986).

When the head moves the eyes rotates in opposite direction to the head movement and maintains focus on the object of interest. This is executed via the vestibulo-ocular reflexes (VOR), which depend on the ability of the vestibular organ to sense head accelerations. When moving the head the semicircular canals detects the angular acceleration of the head and sends excitatory impulses to the corresponding extra ocular

muscles via the vestibular neuron. That means a horizontal head rotation will mainly stimulate the lateral semicircular canal while a head tilt will stimulate the vertical canals. The rotational VOR (r-VOR) stabilize the retinal image during short lasting head turns. Since the semicircular canals are paired, stimulation of the semicircular canals on one side of the head is followed by an inhibition of the corresponding semicircular canal on the contra lateral side.

The translational VOR (t-VOR) stabilizes the retinal image during linear head movements such as when walking (e.g., up- and downward head movements) and is predominantly sensed by the otolith organs in the inner ear. Each side has two otolith maculae, the close to horizontally positioned utricle and the vertically positioned saccule. The utricle responds best to side-to-side head translations and to the pull of gravity. The saccular macula responds best to up and down head movement.

1.4.2 Optokinetic nystagmus (OKN)

When the head is rotated with a constant velocity for a longer period the fluid in the semicircular canals will stop after approx. 6 seconds (time constant; Furman et al. 2003). This means the r-VOR will decay since the vestibular apparatus is not capable of sensing longer lasting head rotations. This requires an assisting system to maintain image stabilizing eye movements when the r-VOR diminishes.

The optokinetic system is sensitive to coherent optical flow on the retina. As the r-VOR response gradually diminish the compensatory eye movements are not compensating enough, leading to image motion on the retina. The optic flow triggers the optokinetic system to take over and maintain the stabilizing eye movements as long as the visual coherent optic flow persist (Waespe et al. 1977a). The close relationship between the optokinetic system and the corresponding vestibular system important for detecting head rotations has been well investigated (Waespe et al. 1977b; Schiff et al. 1988; Yokota et al.1992).

1.5 OCULAR TORSION

An eye rotation around the anterior-posterior axis is termed ocular torsion (OT). OT is regarded as a non-voluntary eye movement although Balliet (Balliet et al. 1978) demonstrated that it is possible to voluntarily control the torsional position after training. OT is normally controlled on an unconscious level and responds to vestibular, proprioceptive and visual sensory input.

A conjugate torsional response of the right and left eye is termed *cycloversion* whereas the disconjugate response is termed *cyclovergence*. The coordination of the eyes are crucial for the binocular function. Spontaneous torsional movements are mostly conjugate whereas the cyclovergence is more stable and relies on background patterns (Van Rijn 1994).

Vestibular input has the most dominant influence on OT. When tilting the head towards the shoulder the OT response (ocular counter-roll; OCR) is mediated by the vertical semicircular canals and maintained by the utricle during sustained head tilt as a result of the change of direction of the gravitational pull. OCR compensates for approx. 10-20% of the tilted head amplitude (Miller et al. 1962; Collewijn et al. 1985; Schworm et al. 2002), which is corresponding to the ocular torsion induced when the whole body is rotated (no neck flexion) in the coronal plane (Morrow et al. 1993; Brodsky et al. 2000). A head tilt has been shown to induce OCR excyclo disconjungacy, which increases with head tilt (Pansell et al. 2003).

The proprioceptive sensory organ has a very small influence on torsional eye movements in healty subjects. Proprioceptive input arising from body tilt only elicits small reflexive eye movements (Mergner et al. 1998, Ott 1992). The functional relevance of these eye movements is still unknown. On the other hand, the influence of visual stimulation on the OT response is more evident and has been studied in a variety of settings.

1.5.1 Visually induced ocular torsion to rotating stimuli

Visually induced OT responds to when viewing something tilted or rotating in the visual field. Duke-Elder reviewed the literature of *pure torsion* in 1949, and concluded that visually induced OT was not an artifact. Brecher (1934) had observed the rotation of the eye about the line of sight by inspecting the conjunctival blood vessels through a telescope. The subject was fixating the center of a rotating disc, made up of black and white sectors. Eye rotation occurred in both eyes with constant amplitude in the same direction as the disc, irrespective the viewing was monocular or binocular (Kertesz et al. 1969).

A visual dispay rotating about the line of sight induces optokinetic torsion nystagmus, tOKN, with a slow phase in the same direction as the stimulus followed by a fast phase

in the opposite direction. This have been confirmed by several studies of Howard and Templeton (Howard et al. 1964), Crone (Crone 1975) and Collewijn, Van der Steen, Ferman and Jansen (Collewijn et al. 1985).

Farooq et al., investigated the relation between stimuli velocities (3-1000 deg/sec) and the tOKN response using a rotating sinusiodal grating pattern. They also investigated the effect of stimulation of the central and peripheral visual field. The tOKN slow phase velocity was shown to be linearly related to the log of the stimuli velocity. The velocity of the slow phase increased as stimuli velocity increased up to 200 deg/sec achiving a maximum response of approx. 3 deg/sec in CW and CCW direction. The maximum gain occurred in response to stimuli velocities of 8 deg/sec with median values of 0.16 for CW stimulation and 0.13 for CCW stimulation. This is a larger gain than what has been found in earlier studies, which might be due to differences in the stimuli used (Farooq 2004).

Chung et al., oscillated a spherical visual display sinuidally (amplitud 10 to 80-degrees) at various frequencies (0.2-2.0 Hz) about the visual axis. They found a higher gain for low stimuli velocities and a decreasing gain for higher frequencies and larger amplitudes. They concluded that the torsional optokinetic nystagmus is a well developed reflex within the range of 0.2-2.0 Hz. They could not find any correlation between the torsional response and circular vection (Cheung et al. 1991).

Visually induced torsion can be induced by a variety of visual stimuli patterns. Van Rijn found no differences in the OT response when comparing the stimuli patterns of gratings, rows of dots, random dots, Escher, stereogram and an owl. A single line was however shown to induce a lower gain. All stimuli subtended a visual angle of approximatly 28-degrees (van Rijn 1992). In contrary to this report a random dot stimulus was shown to induce a peak gain of less than 0.1 (Collewijn et al. 1985; Cheung et al. 1991) whereas those using radiating stripes reported a peak gain responses of 0.1 or greater (Howard et al. 1994; Thilo et al. 1999). Peripheral stimulation has been shown to contribute most to the tOKN response (Farooq et al. 2004). The larger the stimulus is the larger the response becomes. This finding is in agreement with the report of Howard et al., who also found that a central occlusion only leaving a peripheral stimulation reduces the response (Howard et al. 1994).

1.5.2 Visually induced ocular torsion to static tilted stimuli

The above mentioned studies all used dynamically rotating or oscillating stimuli. OT has also been shown to be induced by stationary, no-motion stimuli. Greenberg (1960) and Mesker (1954) reported visually induced eye torsion in the direction of tilted visual stimuli, using a subjective after-image technique. Any torsion that occurs while the after-image is visible will show itself as tilted relative the reference line (Howard et al. 1963). Howard and Templeton criticized this subjective method. They used an objective photographic method to picture the scleral blood vessels with a cross-marked on a divided stick in both sides of the eyes while tilting a vertical line of light. The only thing visible for the subject was the line. The line was seen reflected in a semi-reflecting surface; the camera was out of view behind the surface. They could not find any visually induced torsion (Howard et al. 1964). Later on several research groups could report on visually induced torsion when using objective recording techniques (Hughes 1973; Crone 1975; Goodenough et al. 1979) in agreement with Meskers report. Visually induced torsion was shown in a compensatory direction to the stimuli tilt, but only for a minor portion of the stimuli tilt angle (Hughes 1973; Crone 1975; Goodenough et al. 1979). For details see table 1.

Table 1. Summary of earlier studies in visually induced OT during tilt stimulation

Study	Method	Viewing (mono/bino)	Number of subjects	Stimuli (tilt amp)	Stimuli tilt duration (sec)	OT amp (deg)
Mesker 1953	after image		3	stripes (20)		Yes (0.8)
Greenberg 1960	after image			frame (28)		yes
Howard and Templeton 1964	photo	mono and bino	4	line (10)	10	no
Hughes 1973	photo			line		Yes (0.5)
Crone 1975	photo	bino	4	stripes, (various angles)	few	Yes (1.0)
Goodenough 1978	photo	mono	8	frame (28)	20	Yes (0.29)
Goodenough 1981	photo	mono	8	frame (22.5)	15	Yes (0.45)

A healthy human can accurately set a luminous line to the earth horizontal, within ±2 degrees. There is controversy whether the visual system corrects for changes in ocular torsion position in the perception of line orientation and the extent of this perceptual compensation. A linear relationship between ocular torsion position and the visual orientation with some level of compensation by the visual system has been advocated (Goonetilleke et al. 2008). However, the effect of the vestibular system can not be rouled out when setting the line (Pavlou et al. 2003) neither can the postural system be rouled out. Merker and Held tested three hypotheses about the interaction between visual tilt, head tilt by measuring ocular torsion and the estimation of the visual horizon. The first hypothesis that the visual horizon displacement was secondary to ocular torsion was rejected. The second hypothesis that visual and vestibular signals influence not only eye torsion but also the gravitational reference was also rejected as they did not give the same amount of torsion in response to tilt. The third hypothesis of nonlinear interaction of visual and vestibular signals was supported (Goodenough et al. 1981; Merker et al. 1981). Changes of the OT position alone have been shown to change the perceived orientation of a visual line while settings of a visual line cannot be used to infer perceived postural orientation directly (Wade et al. 1997).

2 AIMS OF THE THESIS

The aim of this thesis is to investigate if ocular torsion can be induced by viewing a visual stimulus that is tilted or rotated away from the position, which is considered as the correct, straight-up position in healthy subjects.

If found to exist, to investigate the effect of different visual stimuli, to prolonged stimulation and to visual stimuli in conflict.

This thesis encloses three papers:

Study I - *Visual spatial clues enhance ocular torsion response during visual tilt*

The purpose of first paper was to investigate the existence of visually induced torsion, analyze the effect of spatial information in the visual stimuli and to different contours on the OT response.

Study II - *Drift of Visually Induced Optostatic Torsion*

The purpose of the second paper was to investigate the effect of stimulus tilt angle and how OT is maintained during continuous stimulation.

Study III - *A rotatory step-ramp paradigm reveals different motion detecting mechanisms for visually induced ocular torsion*

The purpose of the third paper was to investigate if the brain prefers to compensate for stimuli tilt or stimuli rotation by investigating the OT response to a visual a stimuli presenting the tilt and rotation in conflicting directions.

3 MATERIAL AND METHODS

3.1 SUBJECTS

Only healthy subjects with normal binocular function with stereopsis and no history of any ophthalmologic or vestibular disease or medications with a potential influence on visual or vestibular functions were included in the studies. For details see table 2.

Table 2. Description of test subjects for each study

Study	Number of subjects (Male/Female)	Mean age (range)	Range of refractive errors
1	15 (4/11)	28,5 (12-44)	+1.00 to -1.00
2	19 (6/13)	28,0 (21-45)	+1.00 to -2.50
3	16 (8/8)	26,4 (23-32)	+0.75 to -2.00

The research adhered to the tenets of the Helsinki Declaration and was approved by the local ethics committee. The subjects participated with their informed consent.

3.2 EYE MOVEMENT RECORDINGS

Eye movements were recorded binocularly using the Video Oculography (VOG) technique. The 3D-VOG (Senso Motoric Instruments, Berlin, Germany) at 25 Hz (study I and II) and the C-ETD (Chronos Vision, Berlin, Germany) at 100Hz (study III). Video images of both eyes were acquired by two miniaturized video cameras mounted in a head mounted mask (see fig.4). The head mask was firmly attached to the head for individual adjustment to reduce unintended mask movements. The equipment did not allow any glass correction. No contact lenses were used to guarantee the image quality of the iris to be optimal. Horizontal and vertical eye positions were extracted by calculating the pupil position. Ocular torsion was measured by the angular displacement of a defined iris segment. This was achieved by measuring luminance levels of the defined iris segment (profile) and subsequent correlation of the profile with that of each segment for each video frame. The concordance between the initially selected reference profile and that of the same iris segment of each following frame throughout the recording was computed by the software. Torsion data with a quality value of or above 0.3 should be considered for evaluation, because a lower value does not guarantee correct evaluation of torsion. The recordings were digitized and calibrated into ASCII data for the six channels (right and left eye; horizontal, vertical, and torsional data) and imported into analysis software for evaluation (Origin software; Microcal, Northampton, MA).

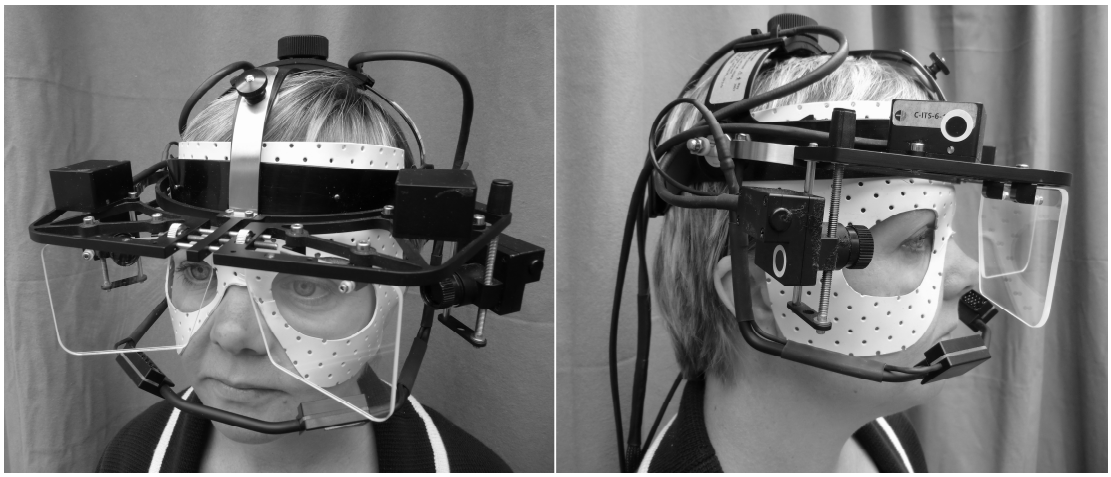

Figure 4. The head mounted video system (C-ETD).

3.3 VISUAL STIMULI AND TEST CONDITION

The visual stimuli was presented on a back-projected screen by a computer projector in the first study while an LCD screen (res 1600x1200px; contrast 900:1, frame rate 60Hz) was used in study II and III.

3.3.1 Study I

Three different visual stimuli were used in study I. The same city scene with buildings and a water front was used twice, first with a square periphery (horizontal visual angle 63-degrees) and then with a circular periphery (horizontal visual angle 50-degrees; see fig. 5 a and b). A square periphery has been shown to induce a stronger sensation of self-tilt compared to a circular periphery surrounded the tilted square (Ebenholtz et al. 1983). We wanted to control for the stimuli periphery when investigating the effect of spatial information on the generation of visually induced OT. The last stimulus displayed yellow rectangles on a black background (horizontal visual angle 63-degrees; see fig. 5 c). This stimulus was intended to clearly display the tilt amplitude but containing less spatial information. All tree stimuli had a red fixation dot in the center.

Figure 5. The three visual stimuli used in the test trials (in color during testing). Stimulus (a) illustrate a photo enriched with spatial clues important for maintaining body posture and with a square periphery (S-SC). Stimulus (b) are the same visual scene with a circular periphery (C-SC), stimulus (c) was constructed with yellow and black squares and contains less spatial information (S-NSC).

The stimulus started with the visual scene in zero position (i.e. no tilt, from now on called 0-degrees) for 30 seconds. The 0-degrees stimulus was then shut off and at the same time a similar stimulus was displayed with the only difference that it was rotated 15-degrees CCW from the subject's point of view around the center fixation dot. This tilted stimulus was displayed for 15 seconds, and then exchanged for a similar stimulus rotated one more 15-degrees CCW to 30-degrees and similarly after 15 seconds to 45-degrees CCW (see fig. 6). After tilting the stimulus in CCW direction the stimulus was again displayed in the 0-degrees position for 15 seconds and a similar procedure was performed while tilting the target CW. The direction of tilt was randomized. Total stimuli time was 160 seconds in all three test conditions.

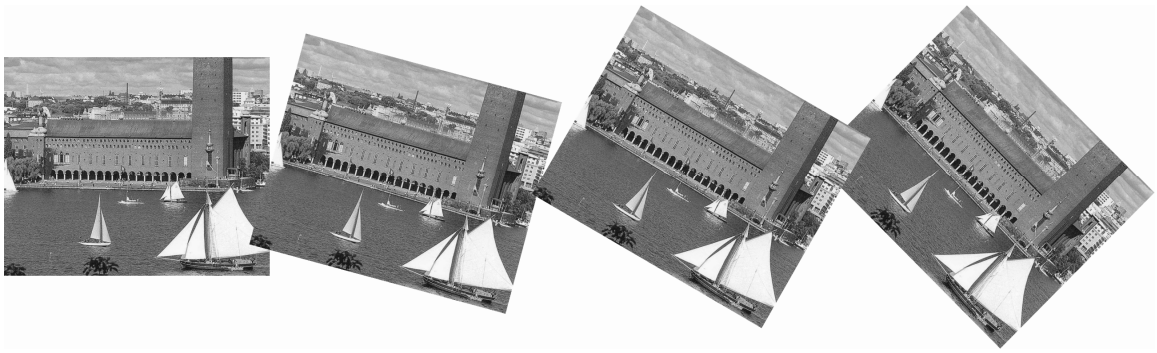

Figure 6. The visual stimulus was first seen in straight position (i.e. no tilt; a) and subsequently tilted to 15 (test a), 30 (test b) and 45-degrees (test c) around the fixation target in the center of the stimulus.

3.3.2 Study II

The city scene with the square periphery was used in all test conditions in study II. Since the visual stimulus now was displayed on the LCD the horizontal visual angle was smaller, 47-degrees. The 0-degree stimulus was after 20 sec shut off and at the same time a similar stimulus was displayed with the only difference that it was tilted either into 15 (test a), 30 (test b) or 45-degrees (test c) CCW depending on the test order. The tilted stimulus was displayed for 4 minutes and 40 seconds. All subjects were exposed to all three test conditions. The a, b and c tests were randomized to

reduce any possible learning effect. The preparation between the tests took approx. one minute and total experiment time was 30 minutes.

3.3.3 Study III

The idea of this study was to investigate the effect of tilt and rotation on the generation of visually induced OT. This was accomplished by using a step-ramp paradigm where the visual stimuli were tilted and rotated in opposite and conflicting directions. The step and ramp stimuli was arranged in two different stimuli, step-ramp (SR) and ramp-step (RS) to correctly evaluate the effect of each stimulus on OT. A photo of an interior room was used as the visual stimulus. The stimulus had a circular periphery and subtended a visual angle of 35-degrees. The stimulus was tilted or rotated around its central fixation point, which coincides with a vase with flowers (see fig. 7).

Figure 7. Photo displaying the visual scene used as stimulus in 0-position. The stimulus was rotated around the geometrical centre of the stimulus close to the flower bouquet. The test subjects were instructed to fixate the bouquet during the whole test. The photo shows *The Ladies' Tearoom* and is used with permission from *The Prince George Ballroom,* New York, USA.

In the SR condition, the stimulus was tilted (step) to a 30-degree angle and then rotated (ramp) back to normal. In the RS condition the stimulus was rotated to a 30-degree angle and then tilted back to 0-degrees. Under both conditions the movements were repeated once. The rotations had a constant velocity of 1.5 deg/sec and the stimulus was displayed in 0-degrees for 10 seconds before and after the movements resulting in duration of 60 seconds for each condition (see fig 8).

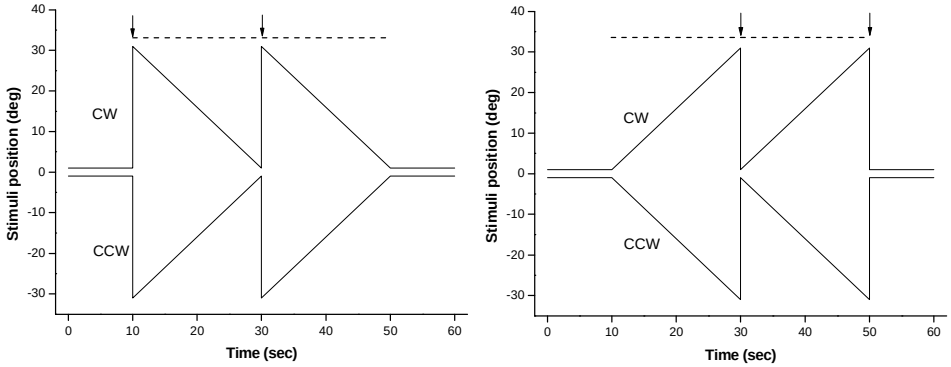

Figure 8. Two graphs illustrating the stimuli position over time. Each graph includes two mirrored position traces in CW and CCW stimuli direction. The first graph displays the SR condition with a shift in stimulus position to 30-degree after 10 seconds in reference position. The stimulus immediately starts to rotate in opposite direction to the tilt towards the reference position (0-position). This was repeated twice. The second graph illustrates the RS condition. The scene starts to rotate after 10 seconds in reference position. At 30-degree position the scene was reset to 0 position and the procedure was repeated a second time. The dashed line in the header marks the period of stimulus rotation (ramp) and the down arrows mark the events of 30-degree position shifts (step). The traces have been separated along the y-axis for clarity

3.4 TEST PROCEDURES

The subject was instructed to pay attention to the whole visual stimulus shown but to have a steady fixation in the centre. The viewing condition was binocular and the investigation room was dark (0.2 cd/m^2) except for the light from the visual stimulus. The subject was seated at a distance of 130 cm from the visual stimuli in study I and at an eye-screen distance of at 50 cm in study II and III. Involuntary changes of head position were prevented with a chin rest and a bite-bar to eliminate VOR. A monocular calibration (amplitude 10 deg and 20 deg in secondary eye positions) was performed prior to testing. All recordings where performed binocularly.

3.5 DATA ACQUISITION AND ANALYSIS

The software provided with the recording equipment digitized and calibrated the video frames into ASCII data for the six channels (right and left eye horizontal, vertical and torsional data). The data was imported into Origin 7 (Origin Lab Corp.) for evaluation. The data was visually inspected and parts containing blinks were identified and manually removed. The signal was smoothed by adjacent averaging (five samples) or a low pass filter (0.1) to reduce signal noise.

3.6 STATISTICS

3.6.1 Study I

The data was converted to positive absolute values and corrected by a square root transformation after inspection of normal probability plots of residuals. An ANOVA for repeated measures analysis was performed. The within-effect of stimuli type (*stimuli*; *S-SC; C-SC and S-NSC*), the direction of the stimuli tilt (*direction*; *CCW* and *CW*) and the amount of stimuli tilt (*angle*; *0, 15, 30* and *45*) was analyzed in the ANOVA model. The variables were analyzed by Mauchley's test of Sphericity for compound symmetry and the results were adjusted by the Huynh-Feldt correction paradigm. Post hoc analysis was performed with the Bonferroni test and a contrast analysis was performed to analyze the least square means in the ANOVA design.

3.6.2 Study II

An ANOVA for repeated measures analysis was performed on the data to analyze the effect of the three levels of stimulus tilt (*angle; 15, 30 and 45*). The data was checked for homogeneous variances to guarantee it was suitable for a parametric test. Post hoc analysis was performed with the Bonferroni test. A linear regression analysis was performed to analyze the correlation between the OT amplitude and OT velocity. A significance level of 0.05 or lower was considered as significant.

3.6.3 Study III

Each step-ramp (SR) and ramp-step (RS) condition resulted in two step measurements (S1 and S2) and two ramp measurements (R1 and R2; see fig. 9). The OT response to steps was measured as the difference in average position immediately before the step and three seconds after the step. The OT response to ramps was measured as the difference in average position three seconds into the ramp and immediately before the end of the ramp. The average OT positions were measured over three second intervals. An ANOVA for repeated measures analysis was performed.

The null hypothesises were that there should be no difference in OT response to CW or CCW direction, that there should be no difference in OT response between SR and RS conditions, that the OT response should not differ from zero within conditions, and that there should be no difference due to presentation order.

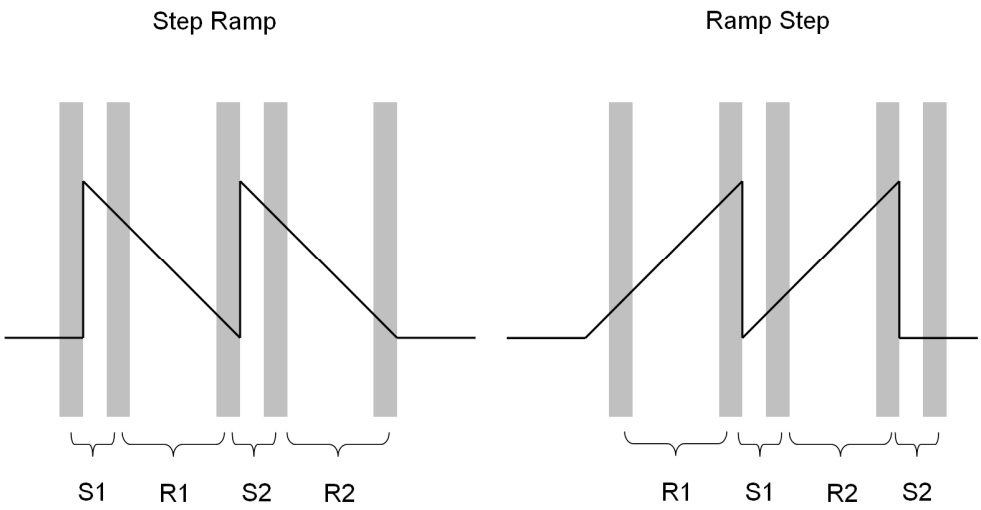

Figure 9. Sample intervals (grey) used to measure OT response for the SR and RS conditions. Stimulus angle on y-axis and time on x-axis. Black trace display stimulus position.

4 RESULTS

The OT eye movements were stable (i.e. no drifts from base line) prior to tilting or rotating the visual stimuli. The right and left OT position was well conjugated during all test conditions close to the spatial resolution of the video system (±0.1 deg) and C-ETD system.

4.1 STUDY I

The purpose of the first study was to investigate the existence of visually induced torsion, then to analyze the effect of spatial information in the visual stimuli and to different peripheral contours. The shift in torsional eye-position was always slow (i.e. 0.1-0.2 deg/s). The largest torsion offset from reference position was 3.5 degrees and occurred to the 45-degrees CCW stimulus in one subject.

4.1.1 Effect of stimuli tilt angle

All subjects displayed a torsional movement in the direction of the tilted visual stimuli. The OT amplitude increased with increasing stimuli tilt angle ($p < .001$; see fig 10). No statistical difference was found between tilting the stimuli in CW or CCW direction ($p = .97$).

4.1.2 Effect of spatial information in the visual stimuli

The stimulus showing the city scene (with spatial clues) induced significantly more OT compared to the stimulus displaying yellow rectangles on a black background (less spatial clues; $p = .022$; see fig 10).

4.1.3 Effect of contours

No difference was found on OT amplitude when analyzing the difference between the square contour and circular contour ($p = .94$; see fig 10).

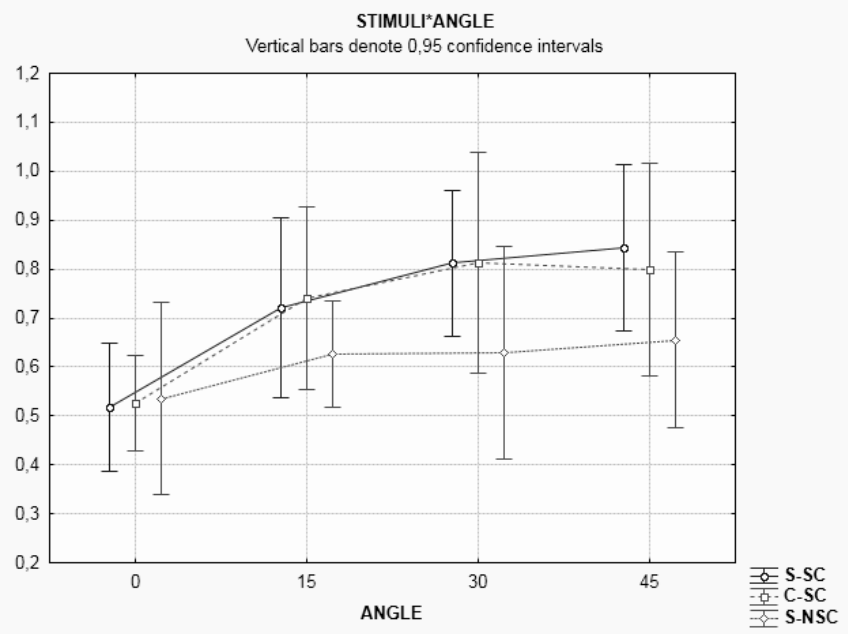

Figure 10. Graph illustrating the average OT response for each stimulus type (S-SC, C-SC and S-NSC) and tilt angle (0, 15, 30 and 45-degrees). The S-NSC stimulus induced less OT compared to the stimulus with spatial clues. The vertical bars denote 95% confidence interval. The data used for the graph has been log transformed for normal distribution.

4.2 STUDY II

The aim of the second paper was to investigate the effect of stimulus tilt angle and how OT is maintained over time. A compensatory OT response was found in all subjects and test conditions. The time taken to reach the initial maximum OT response varied (see table 3). The OT response was always slow (0.1 deg/sec) and the response was not maintained over time but drifted back towards the reference position, seen prior to the stimulus tilt, in all subjects (see fig. 11 a-c).

4.2.1 Effect of stimulus tilt angle

No significant difference was found to the different stimulus tilt angles ($p = .73$). A positive correlation between the OT amplitude and OT velocity was found in response to the 30-degrees stimulus ($p = .01$) but not to the 15-and 45-degree stimulus.

4.2.2 Effect of how OT is maintained over time

The drift started immediately when reaching the maximum OT position or after a time interval (approx. 0-10 secs). The average drift amplitude varied (see table 3) and was not statistically different for the three test conditions ($p = .79$). The time to when the drift settled and the average drift velocity varied (see table 3).

Large inter- individual variation where seen after the drift back. Most subjects displayed a new compensatory OT increase, while come subjects displayed a stable OT position around the reference position.

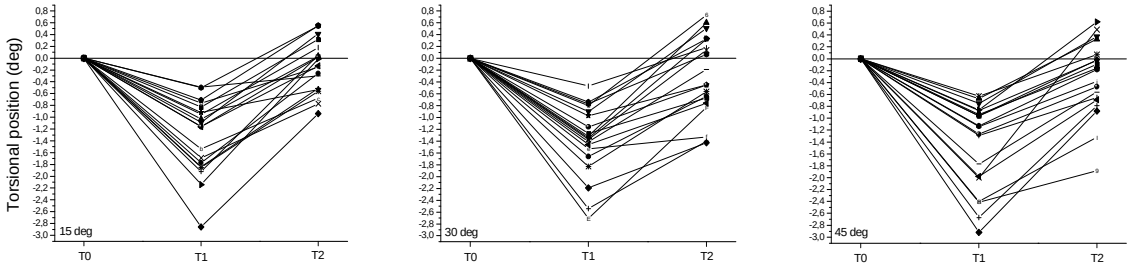

Figure 11 a-c. Three graphs displaying the average initial maximum OT (T1) to the tilted stimulus and the minimum OT position reached after the drift (T2) for all test subjects and test conditions (figure a: 15-degree tilt, figure b: 30-degree tilt, figure c: 45-degree tilt). T0 represent the torsional position the moment when tilting the stimulus and this has been set to zero.

4.2.3 Effect of test order

When analyzing the effect of test order a non- significant but positive trend of increasing OT was found. The OT velocity to the initial OT movement was found to be significant faster for each consecutive test ($p = .046$).

Table 3. Summary of the torsional response to each tilt condition

Tilt amplitude (deg)	Max OT amplitude (deg)	Time to max amplitude (sec)	Drift amplitude (deg)	Time to drift settled (sec)	Drift velocity (deg/sec)
15	1.33 ±0.63	17 ±9	1.18 ±0.49	68 ±27	0.020 ±0.010
30	1.39 ±0.60	15.8 ±7	1.09 ±0.48	66 ±19	0.017 ±0.008
45	1.45 ±0.73	20.6 ±12	1.13 ±0.50	57 ±23	0.023 ±0.016

4.3 STUDY III

The aim of third study was to investigate the OT response to conflicting visual stimuli using a step-ramp paradigm. No significant difference was found in response to CW and CCW stimuli direction for the SR or RS conditions. The CCW data was inverted and analyzed with the CW data. The average OT response for each test condition can be seen in fig.12.

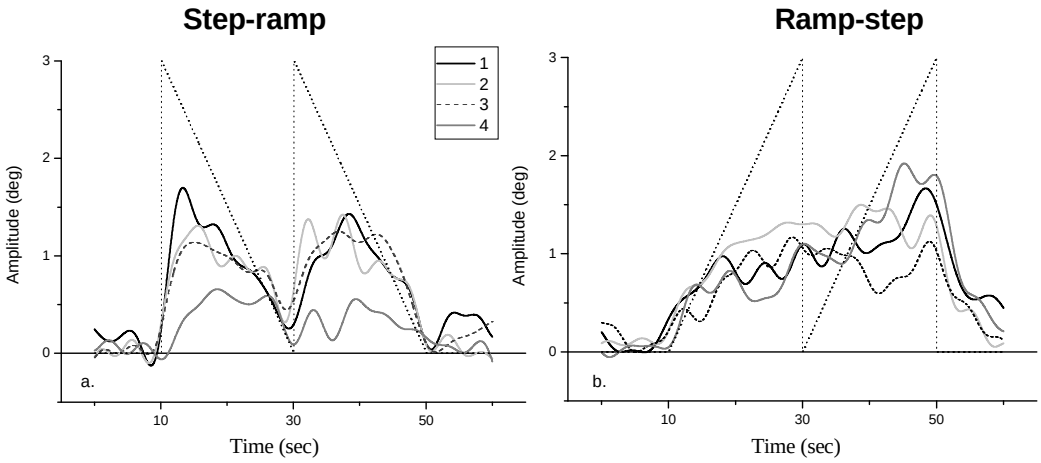

Figure 12. Average OT response for the SR and RS condition. The dotted line represents the stimulus position. The study design randomized *direction* (CW and CCW) and *conditions* (RS and SR), which gave four groups. Line 1 to 4 represents the OT response from each group to clarify the effect of test order.

4.3.1 Effect of condition

A significant difference was found between the SR and RS conditions. Pair-wise comparisons showed that the measurements for S1 were significantly lower for the RS condition ($p < .001$; see fig 13).

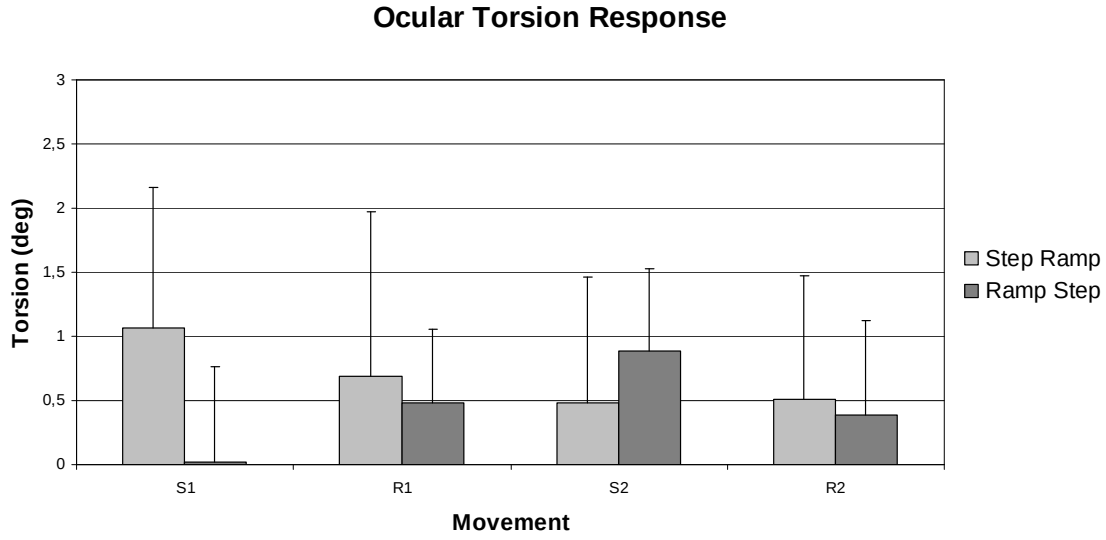

Figure 13. OT response measurements for the SR and RS conditions from each interval used to extract data. Bars represent mean and whiskers indicate standard deviation. The OT responses differed significantly from zero within the SR condition. One-sample t-tests showed that all measurements were significantly different ($p < .008$).

Step-ramp

The first step (S1) induced an OT response in the same direction as the step. The maximal torsional offset from base line was on average 1.4 degrees (SD 1.3) and occurred approx. 3.3 seconds after the stimulus step. After this initial response, in the

same direction as the step, the torsional movement changed direction and returned towards the reference position in the same direction as the ramp (R1). The second stimulus step (S2) occurred at 30 secs, before the torsional position reached the initial reference position. S2 induced a similar torsional response in the same direction as S1 but with slightly smaller amplitude 1.1 degrees (SD 1.7). The torsional position followed the second ramp (R2) back towards the baseline.

Ramp-step

The first ramp (R1) induced a gradually increasing OT response in the same direction as the ramp. The average amplitude in response to the first ramp was 1.0 degree (SD 0.8) in the end of the first ramp at 30-degrees tilt. The OT response to the 30-degree step (S1) was nearly absent. In the average response curve a minor diminution of the OT increase can be seen. The OT increasing drift continued during the following ramp (R2). The largest OT offset from base line was obtained in the end of the second ramp 1.5 degrees (SD 0.9) just before the stimulus was shifted back to the 0-position (S2). The visual stimulus was hereafter held static in 0-position and the OT position returned towards the baseline.

4.3.2 Effect of test order

There was a significant effect of order for the SR condition. The later the SR conditions occurred the less OT was recorded. The effect of order in the RS condition had no significant effect.

5 DISCUSSION

The overall aim of this thesis was to investigate visually induced OT in response to a tilted visual scene enriched with spatial clues important to maintain posture. Tilted visual stimuli induces a very small but still significant amount of OT in the same direction as the visual stimuli, thus in a compensatory direction. This finding is in agreement with several previous reports (Hughes 1973; Crone 1975; Goodenough et al. 1979) who also recognized this torsional response to a static tilted stimuli. We have conducted three studies with the emphasis to investigate the influence of spatial clues on this small OT response and to control for factors such as peripheral shape of the stimuli, amount of tilt angle and the direction of tilt (study I). We have also investigated the effect of prolonged stimulation to evaluate if the induced OT is maintained over time or undergoes some kind of adaptation (study II) similarly to the OCR when tilting the head towards the shoulder. At last we investigated the effect of visual rotation and visual tilt on the OT response (study III) to determine if the brain prefers to compensate for motion or position. Here follows a discussion of each study.

5.1 STUDY I

As the first group we were able to demonstrate that a visual scene enriched with visual objects well known for the test subjects amplified the torsional response when tilting a visual scene. The response was compensatory, but still only for a minor portion of the stimuli tilt. The OT response was very slow. An precise velocity was not posible to compute due to the normally occuring torsional fluctuations as well as the noise in the video signal. The OT amplitude increased with increasing tilt amplitudes and the largest OT offset from baseline was seen in response to the 45-degree stimulus tilt.

The finding of the OT response to a static tilted visual scene supports the idea of an active perceptual mechanism in distinction of the elements presented in the visual scene rather than a reflexive oculomotor response to just a tilted image. The visual stimuli represent objects, which are predetermined by the viewer. The relationship between the well-known elements *water* and *sky* is always the same when the observer is standing upright; the sky is always seen above the water. This response has not a retinal stabilizing function since the stimulus was motionless, but seems to be related to how it is projected onto the retina. One possible mechanisms for this OT response could thus be a primary visual compensatory response to improve visual perceptual processing.

Another possible mechanism could be that a tilt of such a scene might be interpreted as the body was tilted towards the opposite direction. This finding shows that the visually induced torsion share some characteristics with the OCR during head tilt as both compensates in some way to realign the retinal horizon closer to the earth horizon. It is plausible that a common torsional generator exists for both the visually and vestibular induced OT.

5.2 STUDY II

Ocular counter-rolling during head tilt has been shown to adapt and drift back during a sustained head tilt paradigm (Yashiro et al. 1996; Pansell et al. 2006). The question raised in this study was if the visually induced torsion displayed similar characteristics to the OCR with a drift back or if the OT response was maintained on a constant level.

The stimuli were tilted for 4 minutes and 40 seconds, long enough for the OT response to respond and settle. When re-analysing the effect of tilt angle on the OT response we now found a non-significant effect of tilt angle. This finding is in contrary to what was reported in the first study. The reason for the different finding is most certainly the time taken to reach the maximum response. It took approx. 20 seconds and we only used 15 seconds in each stimulus position in study I. The longer tilt durations also gave larger OT amplitudes compared to the first study.

After reaching the maximum response after approx. 20 secs the OT started to drift back towards the baseline. The drift was very slow (0.02 deg/sec) and it took slightly more than a minute until the drift settled. The underlying mechanism for the generation of OT is not clear, nor the reason for the failure to maintain the OT position. One possible mechanism for the drift might be a leaky neural integrator, unable of maintaining the OT response (Robinson 1975). It is however not clear if there exists a neural integrator for OT as for the horizontal and vertical eye movements. The activity of the otolith is supposed to not undergo adaptation (Wade 1970).

The visual system might not be able to recognize the changed image position – nor the slow drift movement on the retina. Furthermore, it is not clear if the muscle proprioceptive mechanism in the extra ocular muscles is capable of sensing an OT drift of 0.02 deg/sec. The lengthening or contraction of the oblique muscles is relatively

smaller during torsional rotations compared to the rectus muscles during horizontal and vertical rotations due to the muscle insertions on the globe.

The OCR drift velocity was similar to the OT drift velocity found in the present study. This finding might indicate a common torsional gaze holding mechanism for maintaining the OT position independent of what afferents inducing the torsional response.

5.3 STUDY III

A sudden tilt of the visual scene is never experienced in normal life. Tilting the head will always induce a rotating optic flow around the fovea. The same applies for when tilting a physical object. The question raised in the third and last study was how CNS reacts to a stimulus with both tilt and rotation. To be able to distinguish between those we constructed a visual target where the rotation and tilt was moving in opposite directions, that is, tilt in CW and rotation in CCW or the other way around. We presume the brain has to decide to what feature it should compensate for or if they will cancel out each other.

In the SR condition OT was initially induced in the same direction as the step, thus in opposite direction to the ramp. The finding of a clear response also to the second step implies that the OT drift seen after the first step event is a feature tracking response rather than compensation to the image motion.

In the RS condition the OT response was induced in the same direction as the ramp, thus in opposite direction to the step. The OT increasing movement disregarded the step event completely, following the rotating visual scene until the end of the task. Based on these findings we believe that a motion sensing system might drive the OT response in response to the RS paradigm.

The SR and RS condition induce completely different torsional responses, which implies that visually induced OT is controlled by two different mechanisms. Which one is controlling the OT movement seems to depend on what feature of the stimulus is starting first.

A fundamental difference between the step and the ramp is that the step will only induce a perceptual impression that the scene has rotated in the absence of any retinal image motion while the ramp induces true retinal image motion.

5.4 GENERAL DISCUSSION AND CONCLUSIONS

Based on the results of this thesis we can draw the following conclusions:

- Visually induced ocular torsion is induced in the same direction as the tilted stimuli. The response amplitude is small and only compensates for a minor portion of the stimuli tilt. The OT velocity is slow, inducing a gradual shift of baseline position. The OT response is well conjugate for the right and left eye.

- Visually induced ocular torsion is amplified when using a visual stimulus enriched with spatial clues. The effect of the peripheral shape of the stimuli has no significant effect on the OT response.

- Visually induced ocular torsion is not maintained over time but drifts back towards the initial reference position during prolonged stimuli tilt.

- Visually induced ocular torsion responds in the same direction as the step in a step-ramp paradigm disregarding the ramp. Visually induced ocular torsion responds in the same direction as the ramp in a ramp-step paradigm disregarding the step.

5.5 WHAT MIGHT FOLLOW?

While several interesting findings have been revealed in this thesis several questions still remain unanswered. How a tilted visual scene is interpreted by CNS is not an easy question to answer and why OT is induced remains unanswered. There is no obvious reason for the brain to compensate for a tilted visual scene. The visual system is certainly capable of decoding the visual scene without the OT response. To continue the exploration of visually induced torsion I would suggest the following topics:

- What happens if the stimulus starts in tilted position without an initial reference position in 0-degree? This question is interesting in understanding to what feature the OT is responding to.
- How sensitive is OT to visual tilt and at what angle is visually OT induced?
- Are there any differences between stimulating the central and peripheral part of the visual field? How small can the stimulus be and still induce OT?
- To explore the influence of visual tilt in patients with reduced vestibular function or in patient with reduced proprioceptive function of the neck?

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